REMARKS

Claims 68, 70-72, 75-80, 82-83, and 85-114 are presently pending in the case. Claims 97-107 and 112-114 are withdrawn. Claims 1-67, 69, 73-74, 81, and 84 stand cancelled. Claim 110 is newly cancelled. Claims 68 and 70 are hereby amended to incorporate the limitations of claim 110. Claims 83, and 108 are hereby amended to correct obvious typographical errors as the claims were previously dependent on cancelled claims and to correct the typographical error in claim 83. Claim 93 is hereby amended to include additional dosages which are fully supported in the specification, for example, in paragraph 108. Upon entry of the amendment, claims 68, 70-72, 75-80, 82-83, 85-96, 108-109 and 111 will be pending and under examination.

Applicant submits that the amendments can be properly considered after final as the amendments do not require further search or consideration of any new issues. Consideration and entry of the amendment into the case is respectfully requested.

Withdrawal of rejections

Referring now to the Office Action, Applicant thanks the Examiner for the withdrawal of the rejection of the claims for obviousness in view of Penkler, sometimes in view of Sallman.

Double patenting rejection

Claims 68, 70-72, 75-80, 82-83, 85-86, 91-92, 95-96, and 108-111 stand rejected on the grounds of nonstatutory obviousnesss-type double patenting over claims 1-3, 8-17, 22-29 and 34-37 of US Patent No. 6,713,089.

The Office Action alleges that claim 1 of the '089 patent covers the claim limitations of solubility, particle size, pKa of the active compound, contacting an aqueous media, particle size of the particulate composition, release rate of the active composition using a specific dissolution method, and the composition comprising a pharmaceutically acceptable excipient. The Office Action further suggests that the difference between claim 1 of the '089 patent and the instant claims is the use of the

term "dissolves" in the instant claims as opposed to the term "releases" in claim 1 of the '089 patent.

Applicant submits that the claims of the instant application are not obvious in view of the claims of the '089 patent

However, upon indication that the remaining rejections have been overcome, Applicant will consider submission of a terminal disclaimer in order to expedite allowance of the application.

Rejection under 35 U.S.C. §103

Claims 68, 70-72, 75-80, 82-83, 85-86, 91-92, 95-96, and 108-111 are rejected under 35 U.S.C. §103(a) over Nemoto et al (JP 03-240729, hereinafter Nemoto). Applicant notes that the reference was referred to as Masami in the parent application.

The Office Action asserts that Nemoto teaches all of the elements of the invention. The Office Action points to the results of Nemoto from solubility tests in artificial gastric juice to demonstrate that the compositions made by the methods of Nemoto have the same properties as the compositions of the instant claims.

Applicant respectfully disagrees. The issue of obviousness in chemical cases has been reviewed by the Courts in view of the recent KSR decision.

> "While the KSR Court rejected a rigid application of the . . . TSM test in an obviousness inquiry, the Court acknowledged the importance of identifying 'a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does' in an obviousness determination."
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> "When there is a design need or market pressure to solve a problem and there is a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp." KSR, 127 S. Ct. at 1732. * * * That is not the case here. Rather than identify predictable solutions for antidiabetic treatment, the prior art disclosed a broad selection of compounds any one of which could have been selected as a lead compound for further investigation. Significantly, the closest prior art compound (compound b, the 6-methyl) exhibited negative properties that

> would have directed one of ordinary skill in the art away from that compound." *Takeda Chemical Industries Ltd. v. Alphapharm Pty*. 492 F.3d 1350 (Fed. Cir. 2007)

Applicant submits that there would be no motivation to modify the methods of Nemoto as they do not provide a problem to be solved. Table 3 on page 9 demonstrates that the methods of Nemoto provide any of a number of compositions that have more than satisfactory dissolution rates in simulated gastric juice using the method provided. Therefore, no design need or market pressure is present. Moreover, the teachings of Nemoto demonstrate variations in the specific components of the compositions, but the methods of making the tablets are the same throughout all of the examples in the reference. Nemoto neither teaches nor suggests that varying the method for tablet preparation could alter dissolution properties, or how one might alter methods of tablet preparation to alter dissolution properties. Therefore, based on the teachings of Nemoto one would not be motivated to vary the methods for preparation of tablets.

In regard to the shortcomings of Nemoto, the Office Action expressly acknowledges that Nemoto does not provide "testing the dissolution of the composition by employing 0.07N HCl as dissolution media." However, the position is taken that it would have been obvious to test the compositions of Nemoto in 0.07N HCl and "produce the instant invention" (page 7).

Applicant submits that the testing method to determine dissolution rate is not an element of the invention, but instead a method to characterize compositions made by the method of the invention. The testing method allows for comparison of the dissolution properties of various compositions to determine if compositions have the desired properties and fall within the scope of the claims. Upon testing, the compositions of Nemoto were found to not meet the dissolution property requirement of the claim. As the composition of Nemoto does not meet the dissolution requirement of the claim, Nemoto cannot render the instant claim obvious.

Moreover, the Nemoto reference was cited in the prosecution of the parent application as noted above. A Declaration was filed by one of the inventors Poul

Bertelsen (copy enclosed) in which the dissolution of a composition made based on the teachings of Nemoto was tested using the method required in the claims of the instant invention. The results are provided in Appendix A of the Declaration. After 1 hour, the composition made according to the teachings of Nemoto with a 1:5 ratio of oxicam to antiacid was found to release only 37.8% in 0.07N HCl. Therefore, the amount released after 20 minutes must have been less than 50% as required by the instant claims. The composition with a 1:5 ratio of oxicam to antacid when tested by Nemoto dissolved 73.5% in 20 minutes. This demonstrate that the results from the testing method of Nemoto do not predict the results from the testing method required by the claims.

The Declaration of Poul Bertelsen further discusses other aspects of the invention in the currently pending dependent claims that further differentiate the instant invention from the Nemoto reference.

Paragraphs 5-8 of the Bertelsen Declaration discuss the differences between the particulate composition recited in the claimed methods (e.g., in currently amended claims 68 and 70) and the methods of Nemoto. Nemoto teaches granulation, which includes preparation of aggregates to make larger particles more suitable for compression into tablets. Specifically, the Mesh 20 used by Nemoto (last sentence on page 5) corresponds to a particle size of 800 µM. The Leiberman reference provided with the Declaration demonstrates that those skilled in the art considered that enlarging particles into aggregates is performed to "render the material free flowing." This was also a goal of the granulation step of Nemoto who performed the granulation step for "the production of granules having good fluidity" (second full paragraph, page 3). Nemoto frequently comments about the inappropriateness of certain combinations of antacid and oxicams as they result in problems forming tablets as they crack or chip during coating (see, e.g., last sentence on page 2, last sentence of second full paragraph page 3). These are problems that one would expect to have if the components to be included in the tablet had not undergone proper granulation and were too small (e.g., see first paragraph of IV. Granulation in Leiberman).

Examples 15-17 and Tables 8-10 of the instant application demonstrate that the use of particles that pass through a 180 µM sieve or have a mean particle size of at the most 250 µM, which is far smaller than is either taught or suggested by Nemoto, results in a final composition with a high dissolution rate. Applicant submits that based on the teachings of Nemoto, one would not be motivated to make the instantly claimed compositions having a small particle size. The rejection of claim 110 (the limitations of which are now incorporated into claims 68 and 70) set forth in the Office Action does not consider the size limitation included in the claim (page 9). Instead the Office Action states that the use of the dissolution test of the claims would have been obvious in view of the dissolution test of Nemoto. Reconsideration is requested.

Claims 87-90 and 93-94 are rejected for alleged obviousness over Nemoto further in view of Penkler (US 5,854,226, hereinafter the '226 patent).

The '226 patent does not remedy the deficiencies of Nemoto. The documents, even in combination, fail to teach or suggest the feature of the invention wherein the particles of the particulate composition used in the manufacture of the composition pass through a 180 µM sieve or have a mean particle size of at most 250 µM. As discussed above, the Nemoto requires the formation of large granules for the preparation of tablet compositions. The '226 patent provides no suggestion which would cause one skilled in the art to modify the teachings of Nemoto to use a particulate composition used in the manufacture of the composition pass through a 180 µM sieve or have a mean particle size of at most 250 µM, as claimed presently. The rejection is therefore properly withdrawn.

There is no suggestion or motivation, either in the reference(s) themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the cited reference(s) to make the claimed invention, nor is there a reasonable expectation of success.

In view of the above amendments and remarks, Applicant believes the pending application is in condition for allowance.

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Respectfully submitted,

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